

Serial No. 10/734,731
Attorney Docket No. 029310.52995US

REMARKS

Favorable consideration and allowance are respectfully requested for claims 1-14 in view of the foregoing amendments and the following remarks.

The rejection of claims 1-4, 7-12 and 14-15 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement for a method for detecting a pain-regulating substance is respectfully traversed.

The standard for adequate enablement is whether the specification describes the claimed subject matter in such a way as to enable a person skilled in the art to which it pertains to use the invention. Thus, enablement is judged in view of the combined teachings of the specification and the knowledge of one skilled in the art.

The specification describes that the inventors undertook to identify pain-regulated genes which are modified in their expression under pain conditions and that these genes are thought to be involved in the development and processing of chronic pain, see paragraph [0007] of the specification. Upon identification of these genes, methods of detecting pain-regulating substances may be performed by testing potential pain-regulating substances for its capacity to bind the protein produced by these genes or by measuring functional parameters modified by the binding of the test substance.

The specification describes numerous tests which were performed in order to identify certain proteins as relevant to pain. These include tests related to CFA-induced polyarthritis (beginning at paragraph [0086]) with differential display RT-PCR; CIA-induced arthritis (beginning at paragraph [0099]) with immunocytochemical staining; differential expression between DNPI and BNPI via immunocytochemical staining (beginning at paragraph [00103]). These experimental results show that the expression levels of BNPI *is increased* under experimental pain conditions.

The Office Action asserts that "a change in expression of one protein . . . in an animal model of pain does not indicate that expression of that protein is

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linked to pain." The Office Action then continues in that paragraph to conclude that "That does not mean elevated Vglut1 causes pain." This misses the point of the present invention, which is directed, in part, to identifying compounds which interact with a protein having a regulating influence on the physiological pain event, see paragraph [0011]. This does not mean that one must first conclude that Vglut1 causes pain. Instead, one must understand that Vglut1 has some role in pain, for instance enhancing the perception of pain.

The U.S. Court of Customs and Patent Appeals has stated that "The first paragraph of § 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 USPQ 367 , 369 (CCPA 1971). The court also added that "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." *In re Marzocchi*, 169 USPQ 367 , 370 (CCPA 1971). The present record does not explain why the experimental results, which show that BNPI expression is enhanced in experimental pain models, should not be understood to indicate that expression of that protein is linked to pain.

Instead, the Office Action makes the conclusory assertion that enhanced BNPI expression may have nothing to do with pain. The law makes clear that patent applicants may satisfy their burden of enablement simply through objective statements. In the present instance, not only have applicants provided such objective enablement, applicants also provided results from four different sets of experiments, all of which show that BNPI is relevant to pain.

The Office Action does not explain why one of skill in the art would doubt the truth of the assertions in the specification, and instead simply concludes that the evidence does not adequately show the nexus between BNPI and pain and

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then secondly that, as a result, further experimentation is necessary. This heightened standard for enablement is improper and not supported in the law. As a result, the Office Action has failed to lay out a proper enablement rejection.

There is nothing in the record to suggest any reason why the method would not work as claimed. Indeed, based on the knowledge of a person of skill in the art and the evidence provided in the Examples provided in the present specification, a person of ordinary skill in the art would conclude that all of the claimed methods would be operable.

As indicated above, the burden is on the Patent Office to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. On the present record there is no such explanation, and no apparent reason is offered to support the notion that the statements in the specification are not true or accurate. Instead, conclusory assertions are provided. Moreover, the present record provides ample evidence that the claimed compounds would be active for the claimed methods.

The Office Action discusses the Sun reference and concludes that the art does not recognize that upregulation is predictive of causality. As indicated above, the point is not that BNPI *causes* pain, but instead that it plays some role in pain. As indicated in the Office Action, the Sun reference was aimed at identifying "genes that are enriched in the dorsal spinal cord *that can potentially play important roles* in pain transmission, pain modulation and pathophysiological conditions" (emphasis in Office Action). Thus, the reference indicates that these substances are pain-relevant. The relevance of the substance to pain is provided through the substance's capacity to bind proteins which are modified in their expression under pain conditions, or modify other functional parameters by their binding. No further experimentation is required to understand or confirm that BNPI has some relevance to pain.

In sum, the Office Action concludes that Vglut1 has no relevance to pain, and offers no evidence which shows that Vglut1 was tested for relevance to pain

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and found to not have relevance. Instead, the Office Action asserts that Sun's failure to identified Vglut1 as pain relevant means there is no nexus. This requires the unreasonable assumption that Sun has identified every possible protein that might be relevant to pain. While Sun may have identified many, it certainly did not identify every pain relevant protein.

For the foregoing reasons, a person of skill in the art would be able to practice the claimed invention without further undue experimentation. Accordingly, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. § 112, first paragraph, are respectfully requested.

The Office Action recasts the prior written description rejection of claims 1-4, 7-12 and 14-15 into an enablement rejection under 35 U.S.C. § 112, first paragraph. As such, the finality of the Office Action should be withdrawn. This new rejection is respectfully traversed.

As amended, claim 1 clarifies that "measuring said functional parameter involves measuring the regulation, inhibition or activation of receptors, ion channels or enzymes or via measurement of a modification in gene expression, ionic milieu, pH or membrane potential, or via a modification in enzyme activity or concentration of a second messenger." Support for this amendment is provided in the specification, at least at page 23, second paragraph.

To the extent the rejection is based on the perceived breadth of the "functional parameter terminology", applicants note that the claim language now clearly defines the scope of the function parameters. Like the enablement rejection addressed above, the Office Action fails to *explain* why one of skill in the art would not be able to make and use the claimed invention.

The present specification provides clear support for the claimed methods such that one of skill in the art could readily practice the methods. The claims themselves adequately define the methods with such particularity that one of skill in the art would not have to "envision" any steps. Instead, the person of skill in the art could readily review the specification and claims and begin to

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practice the claimed method. Accordingly, the claims are properly enabled, and reconsideration and withdrawal of this rejection are respectfully requested.

The rejection of claims 1-4, 7-12 and 14-15 under 35 U.S.C. § 112, second paragraph, as indefinite, is respectfully traversed.

As amended, the claims recite step "(c) determining whether the test substance is a pain-regulating substance." On page 9 the specification indicates that pain regulating means directly or indirectly influencing the perception of pain. Thus, one practicing the method will actually determine whether or not the substance influences the perception of pain. A person of skill in the art would have no trouble in determining the scope of the claim. Accordingly, the claim language accurately and definitely describes the claimed invention.

The Office Action asserts that the phrase "stringent conditions" is not defined in the specification. Claim 1 is amended to delete the reference to the stringent conditions and instead recites that the nucleic acid is the reverse complement of one of the listed polynucleotides. There is nothing indefinite about this claim language.

The Office Action also asserts that claim 1 is indefinite because it is unclear whether step (b) is practiced with the biomolecule of step (a) or only with a cell synthesizing the biomolecule. Step (b) recites "measuring the binding of the test substance to the protein or part protein synthesized by the cell *or* measuring at least one functional parameter modified by the binding of the test substance to the protein or part protein" (emphasis added). The presence of the highlighted "or" shows that the claim contemplates methods including either of these alternatives. The use of alternative language is widely accepted practice in patent claim drafting. There is nothing indefinite about the present claim language.

The Office Action also asserts that claim 1 is indefinite because it omits a step of "determining if the compound has detected a pain regulating substance." As amended, the claims now recite this step. Accordingly, this allegedly missing step is provided in the method.

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The Office Action also asserts that claim 1 is indefinite for using the term "functional parameter". The functional parameters are specifically defined in claim 1, as amended. In view of this amendment, reconsideration and withdrawal of this rejection are respectfully requested.

Claims 2-4 and 7 are alleged to be indefinite for reciting "genetic engineering." This phrase is commonly known and widely used by persons of skill in the art. The claims are amended to provide the meaning of the term therein. Accordingly, a person of skill in the art would readily understand the claim and reconsideration and withdrawal of the rejection are respectfully requested.

Claim 4 is allegedly indefinite for reciting expression of a G protein. The meaning of the term G protein is provided in the specification on page 21 which indicates that it is a GTP-binding protein. The Office Action asserts that it is not evident how this limitation of claim 4 relates to the claimed method. Reviewing the claims, they clearly show how the limitation relates to the claimed method. In particular, the claims state that the manipulation by genetic engineering of claim 3 causes expression of a form of a G protein. Claim 4 depends from claims 1-3, which recite that the cell is manipulated by genetic engineering and that this allows for the measurement of at least one functional parameter modified by the binding of the test substance.

A person of skill in the art could readily determine the scope of claim 4, and accordingly it meets the requirements for definiteness. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-5, 7-12 and 14-15 are allegedly indefinite for reciting a "ionic medium". As amended, the word "medium" is replaced with "milieu". Thus, the objected-to phrase does not appear in the claim and reconsideration and withdrawal of this rejection are respectfully requested.

In view of the foregoing, reconsideration and withdrawal of all of the indefiniteness rejections are respectfully requested.

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The rejection of claims 1-3, 7-12 and 14 under 35 U.S.C. § 102(e) as anticipated by Edwards et. al. (US 2002/0098473) is respectfully traversed.

The present claims recite the step of "(c) determining whether the test substance is a pain-regulating substance." Accordingly, any reference which might anticipate the claims would have to include this step.

The provisional application from which the cited reference claims priority does not appear to contain the portions of the reference disclosure relied on in the Office Action. The provisional application does not mention pain or management of pain in any way. Accordingly, for purposes of information relied on in the rejection, the reference would not be entitled to an effective date earlier than its July 24, 2001 actual U.S. filing date.

The present application claims priority to German Application No. 101 28 641.3 which was originally filed June 13, 2001. Accordingly, the 102(e) date of the reference postdates the invention date of the present application and the anticipation rejection cannot, therefore, be properly maintained. A certified translation of the priority document is already of record. Reconsideration and withdrawal of this rejection are respectfully requested.

CONCLUSION

In view of the foregoing, the application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

Although an Extension of Time is submitted herewith, if necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any

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deficiency in fees or credit any overpayments to Deposit Account No. 05-1323
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Respectfully submitted,

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